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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,215	03/27/2001	Scott A. Waldman	08321-0166 US	2195

35148 7590 01/24/2005

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EXAMINER	
CALAMITA, HEATHER	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/820,215	WALDMAN ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-11,13-15 and 37-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-11,13-15 and 37-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Amendments of December 6, 2004, have been received and entered in full. Claims 1, 3, 4, 6-11, 13-15 and 37-47 are under examination.

Response to Amendment

2. The objection to claim 2 is moot due to cancellation of the claim. The objection to the specification, and the 112 second paragraph rejections are withdrawn in response to the amendment.

New Matter

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 4 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 4 has been amended to (and newly added Claim 40) recite, "the disseminated epithelial cell marker consisting of "guanylyl cyclase, Cdx-1...tyrosine hyroxylase, and neuron-specific glycoprotein". That is, Claim 4 has been amended (and Claim 40 newly added) to assert that all of the markers listed in these claims are "epithelial" cell markers. However, neither the specification nor the claims previously asserted that all of the markers in Claim 4 (or Claim 40) are considered to be "epithelial" cell markers. For example, on page 12, lines 10-27, the specification only refers to the markers listed in Claim 4 (and Claim 40) as "disseminated cell markers", but not specifically, that the

markers are "epithelial" cell markers. Furthermore, on page 10, lines 7-10, the specification states, "epithelial cell-specific markers including GC-C, prostate-specific antigen (PSA), prostate-specific membrane antigen (PSM), carcinoembryonic antigen (CEA), cytokeratin-19 (CK-19), cytokeratin-20 (CK-20), mucin 1 (MUC-1), and gastrointestinal-associated antigen (GA733.2)." Accordingly, while the specification provides support for the assertion that the markers listed on page 10, lines 7-10, are "epithelial" cell markers, the specification does not provide support for the newly amended Claim 4 (or newly added Claim 40), which assert that markers other than those listed on page 10, lines 7-10, are "epithelial" cell markers.

If Applicants' traverse this rejection, Applicants' should specifically point out (by page and line number), where there is support for newly amended Claim 4 (and newly added Claim 40).

Written Description

5. Claims 1-4, 6-11, 13-15 and 37-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of detecting the presence of *a disseminated epithelial cell marker* in a sample comprising the steps of

a) eliminating CD34+ cells from the sample; and

b) *detecting the presence of mRNA that encodes the marker, wherein the marker is a differentiation-specific antigen.*

(emphasis added).

Thus, the claims are drawn to methods of detecting "disseminated epithelial cell markers", wherein after the elimination of CD34+ cells, "mRNA that encodes the marker, wherein the marker is a

differentiation-specific antigen" is detected. Accordingly, the claims are drawn to detecting the genus of "mRNA that encodes a disseminated epithelial marker, wherein the marker is differentiation specific".

This genus comprises the class of compounds (mRNAs) that share a function (encoding a disseminated epithelial cell marker, wherein the marker is a differentiation-specific antigen). However, the specification does not specify a common structure of this class of mRNAs. That is, while the members of the genus encompassed by the claims (e.g., the mRNA encoding a disseminated epithelial cell marker, wherein the marker is a differentiation-specific antigen), share a function, they do not share a structure that is similar. Each mRNA encompassed by the genus will have different structure, absent any disclosed structural similarities provided by the specification. That is, even assuming, the mRNAs encompassed by the genus are functionally similar, they are not structurally similar, and therefore, the functional description of the mRNAs does not provide adequate written description to the plurality of other structurally distinct mRNAs that are encompassed by the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." (emphasis added)

Additionally, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula,

chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the specification teaches eight epithelial cell markers (see page 10, lines 7-10), and asserts these epithelial cell markers "can be" used as disseminated markers (see page 12, lines 10-27). However, these markers are not structurally related, nor do they share any common sequences, and therefore, these eight species are not considered to be a representative number of species. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., similar structural motifs, sequence similarity, etc.). In the instant case, no such identifying characteristics have been provided for any of the claimed nucleic acids. Furthermore, it is noted that the specification does not describe which mRNA are specific for which "differentiation-specific antigen". In other words, the specification does not describe which mRNAs are specific for a particular tissue-specific marker.

Accordingly, because the specification does make clear that Applicants were in possession of the genus of mRNAs that encode disseminated epithelial cell markers, wherein the cell markers are differentiation-specific antigens, at the time the application was filed, the claims lack adequate written description.

Applicant's attention is also drawn to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1st Paragraph, Written Description Requirement" (published in Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Zippelius et al. (Journal of Clinical Oncology (1997) 15(7): 2701-2708, cited in the IDS).

Regarding, Claims 1-4 and 13, Zippelius teaches methods of detecting the presence of a disseminated epithelial cell marker (e.g., CEA, erb-B2, erb-B3, CK-18, PSM) in a sample comprising the steps of

a) eliminating CD34+ cells from the sample (e.g., removing a fraction of mononuclear cells (which comprise CD+34 cells) before RT-PCR, see page 2702, column 1, under section titled, "Patients and BM Preparation"); and

b) detecting the presence of mRNA that encodes the marker, wherein the marker is a differentiation-specific antigen (e.g., prostate or breast).

(see abstract and pages 2702-3).

It is noted that the removal of mononuclear cells before RT-PCR meets the limitation of "eliminating CD34+ cells", since mononuclear cells from bone marrow will contain CD34+ cells. Furthermore, the claims are drawn to "eliminating CD34+ cells", which can be interpreted as only eliminating a fraction of the mononuclear cells.

Regarding Claims 7-8, the sample was bone marrow (see abstract and page 2702).

Regarding Claims 9-11, mRNA is detected by a "nested" RT-PCR (see pages 2702-3).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-11, 13, 37-40 and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ts'o et al. (USPN 5,962,237), in view of Palsson, B. (USPN 5,874,266).

Ts'o teaches methods of isolating and enriching rare cells (i.e., tumor cells) from body fluids (e.g., blood), by negative selection of non-tumor cells such as white blood cells from the CD family (see

abstract, col. 1, lines 8-13, and col. 5, lines 40-51, col. 10, line 5 to col. 12, line 35, see also generally, cols. 2-5 and 11-16).

Regarding, Claims 1-4, 13, 37-40 and 45, Ts'o teaches methods of detecting the presence of a disseminated epithelial cell marker (e.g., PSA and PSM) in a sample comprising the steps of

a) eliminating nucleated white blood cells (e.g., mononuclear cells and cells from the CD family) from the sample (col. 1, lines 8-13, and col. 5, lines 40-51, col. 10, line 5 to col. 12, line 35); and

b) detecting the presence of mRNA that encodes the marker, wherein the marker is a differentiation-specific antigen (e.g., prostate) (col. 14-16, for example).

Regarding Claims 7-8, the sample was blood (col. 5, lines 48-51, for example).

Regarding Claims 9-11 and 42-44, mRNA is detected by a "nested" RT-PCR (col. 16, lines 47-65, for example).

Ts'o also teaches,

> The rare cells enriched according to this embodiment are substantially free of contamination by non-rare cells. For example, *in the case of the separation of cancer cells from blood, it was found that the cancer cells could be almost completely separated from nucleated white blood cells. This can be advantageous because nucleated white blood cells, if present, can interfere with cell identification, particularly for some of the embodiments wherein polymerase chain reaction (PCR) methods are used.*
>
> For some of the embodiments wherein the fluid comprising rare cells and non-rare cells is blood, *it may be desirable to use antibodies that bind to white blood cells (leukocytes)* and/or red blood cells (erythrocytes). *Examples of suitable leukocyte antibodies include the human and anti-human leukocyte CD antibodies*, e.g., CD2, CD3, CD4, CD5, CD7, CD8, CD11a, CD11b, CD11c, CD14, CD15, CD16, CD19, CD20, CD28, CD36, CD42a, CD43, CD44, CD45, CD45R, CD45RA, CD45RB, CD45RO, CD57, and CD61 antibodies, *and the like.*

(emphasis added) (col. 11, line 53 to col. 12, line 4).

Accordingly, Ts'o teaches that it is advantageous to eliminate mononuclear white blood cells (e.g., cells from the CD family) from the cancer cells because these mononuclear white blood cells cause contamination (e.g., illegitimate transcription) during PCR assays and analysis. Ts'o teaches eliminating members of the CD cell family are desirable, but does not teach removing CD34+ cells.

However, Palsson teaches eliminating CD34+ cells from tumor cells is advantageous to ensure isolation of only the tumor cells (col. 2, lines 21-31). Palsson also teaches that this negative CD34+ selection can be used in conjunction with detection of epithelial cell markers (col. 2, lines 31-34).

Accordingly, in view of the teachings of Palsson, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Ts'o so as to have eliminated CD34+ cells from rare cancer cells. One of ordinary skill in the art would have been motivated to modify the method of Ts'o to have eliminated CD34+ cells, in order to have achieved the benefit of providing a more effective means of detecting epithelial cell markers by reducing contamination caused by the CD34+ cells.

10. Claims 6 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ts'o et al. (USPN 5,962,237), in view of Palsson, B. (USPN 5,874,266), as applied to Claims 1-4, 7-11, 13, 37-40 and 42-45 above, and in further view of

The teachings of Ts'o and Palsson are presented above. The references teach methods of detecting epithelial cell markers, comprising eliminating CD34+ cells, and detecting mRNA encoding said cell marker, wherein said cell marker is a differentiation-specific antigen. The references teach eliminating the CD34+ cells using anti-CD34 antibodies attached to immunoaffinity beads. The references do not specify that this method of using beads and anti-CD34 antibodies is a method of column chromatography.

However, Elliot teaches the elimination of CD34+ using a CD34 Progenitor Cell Isolation Kit (QBend/10) made by Miltenyi Biotech GmbH, wherein "cells are tagged with an anti CD34 monoclonal antibody they were then bound to magnetic microspheres according to protocol. The tagged cells were next passed through pre-filled MiniMacs separation columns, the columns were washed and the CD34+ cells were then eluted from the column." (col. 22, lines 34-41). Elliot teaches this column chromatography protocol results in higher purity isolation of the CD34+ cells.

Accordingly, in view of the teachings of Elliot, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Ts'o and Palsson so as to have used column chromatography for eliminating the CD34+ cells. One of ordinary skill in the art would have been motivated to modify the method of Ts'o and Palsson in order to have achieved the benefit of providing a more effective means of isolating and diluting out the CD34+ cells to ensure a better isolation and analysis of the rare tumor cells.

11. Claims 14-15 and 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ts'o et al. (USPN 5,962,237), in view of Palsson, B. (USPN 5,874,266), as applied to Claims 1-4, 7-11, 13, 37-40 and 42-45 above, and in further view of Waldman et al. (Cancer Epidemiology, Biomarkers & Prevention (1998) 1: 505-514, cited in the IDS).

The teachings of Ts'o and Palsson are presented above. The references teach methods of detecting epithelial cell markers, comprising eliminating CD34+ cells, and detecting mRNA encoding said cell marker, wherein said cell marker is a differentiation-specific antigen. The references teach the rare cells can be epithelial cells (i.e., comprising epithelial cell markers, such as PSA and PSM, see col. 13, lines 56-67, for example), but do not teach the method wherein the epithelial cell marker is GC-C.

However, Waldman teaches the detection of GC-C, which is an epithelial cell marker for colorectal cancer, and can be used in diagnosing colorectal cancer, one of the most common forms of cancer (see abstract, page 505, 1st column and pages 510 and 512).

Accordingly, in view of the teachings of Waldman, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Ts'o and Palsson so as to have detected the epithelial marker, GC-C. One of ordinary skill in the art would have been motivated to modify the method of Ts'o and Palsson in order to have achieved the benefit of providing a means of diagnosing colorectal cancer, which is one of the most common forms of cancer.

Response to Arguments

12. With respect to the enablement rejections of claims 1-4, 6-11, 13-15 and 37-47, applicant's arguments filed December 6, 2004, have been fully considered and are persuasive. Therefore the enablement rejections of claims 1-4, 6-11, 13-15 and 37-47 have been withdrawn.

15. Applicant's arguments filed December 6, 2004 have been fully considered but they are not persuasive.

With respect to the new matter rejections of claims 4 and 40, applicant argues the markers recited in these claims are inherently epithelial cell markers and that one of skill in the art would recognize them as such. Applicant further submits a declaration stating the aforementioned markers are epithelial cell markers, and therefore asserts claims 4 and 40 do not introduce new matter. However, applicant provided no evidence (i.e. published journal articles) with the declaration to support the assertion that the specified markers are inherently epithelial cell markers and that these markers are well known as epithelial cell markers to those of skill in the art. The new matter rejection is therefore hereby maintained.

16. With respect to the written description rejections of claims 1-4, 6-11, 13-15 and 37-47, applicant argues the disclosure describes a representative number (26) species of the genus. However, applicant fails to describe a representative number of species for this genus. The genus is comprised of about 20,000 known human genes of which an unknown number are epithelial cell markers. Applicant has adequately described only 26, or less than 0.2 %. Less than 0.2 % is not a representative number of species for this genus, therefore the written description rejection hereby maintained.

17. With respect to the 102 rejections applicant argues Zippelius et al. does not anticipate the claims of the instant invention because Zippelius et al. do not teach the elimination of CD34+ cells. However, Zippelius et al. teach the removal of mononuclear cells from the sample, and CD34+ cells inherently comprise mononuclear cells. Applicant appears to further argue the removal of mononuclear cells does

not meet the claim limitation, however Zippelius et al. does meet the method steps as claimed. Zippelius et al. teach MNC were isolated by density gradient centrifugation, this meets the claim language of "eliminating CD343+ cells", since mononuclear cells will contain CD34+ cells.

18. With respect to the 103 rejections applicant argues no motivation to combine, Palsson et al teach away from eliminating CD34+ cells and the combination would not lead to the claimed invention. However, Ts'o et al. teach removal of mononuclear cells and Palsson is relied on to exemplify CD34+ cells in particular. Ts'o et al. by state the advantage of removing nucleated white blood cells (i.e. mononuclear cells) because the presence of these cells can interfere with cell identification, particularly for methods such as PCR, and further provides numerous examples of specific mononuclear cell types (see col. 11 lines 58-61, 67 and col. 12 lines 1-5). Palsson et al. exemplify a known specific type of mononuclear cell CD34+ and describe a method using antibodies specific to CD34+ as a means to specifically capture and remove these cells from samples, as suggested by Ts'o. Applicant further argues the references do not motivate one of skill in the art to remove CD34+ cells to remove the high false positive rate that was associated with detection methods prior to the invention. However, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

19. With respect to the 103 rejection of claims 6, 14, 15, 41, 46 and 47, applicant argues the examiner's conclusion of obviousness is based upon the improper application of the combination of the teachings of Ts'o et al. and Palsson et al. Applicant's arguments with respect to these rejections have been considered but are moot in view of the clarification of the application of the combination of the teachings of Ts'o and Palsson.

Conclusion

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita, Ph.D. whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday thru Thursday 7:00 A.M. - 5:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571.272.0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

1/13/05

hgc